In response to the above rejections and in connection with the filing of a Request for Continued Examination (RCE) pursuant to 37 C.F.R. §1.114, Applicants have amended the claims which, when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

In the first instance, Applicants respectfully submit that the Sequence Listing has been amended to correct certain typographical errors. More specifically, Applicants have corrected two typographical errors in the nucleotide sequence of SEQ ID NO: 6 (human bcl-w) at nucleotide position 301, 404 and 405, as indicated in the attached marked-up copy of the amended Sequence Listing. Furthermore, the protein sequence in SEQ ID NO: 7 has been amended to correct two clerical errors appearing at positions 101 and 135. In addition, Applicants have corrected certain typographical errors in the nucleotide sequence of SEQ ID NO: 8 (murine bcl-w), as indicated in the attached marked-up copy of the amended Sequence Listing. The protein sequence in SEQ ID NO: 9 has been amended to correct certain clerical errors, as indicated in the attached marked-up copy of the amended sequence listing.

Applicants respectfully submit that the foregoing amendment does not introduce new matter. More specifically, the protein sequence of SEQ ID NO: 7 (human bcl-w) as amended is set forth in Figure 8 as originally filed. The protein sequence of SEQ ID NO: 9 (murine bcl-w) as amended is set forth in Figure 1 as originally filed. In addition, these protein sequences find support in Figures 9A and 9B of the priority document, Australian Provisional Application PN8965, filed on March 27, 1996. A courtesy copy of such priority document is enclosed for the Examiner's convenience (Exhibit A). The nucleotide sequences of SEQ ID NO: 6 and SEQ ID

NO: 8 as amended are also disclosed in Figure 9A and 9B, respectively, of the priority document.

Applicants further respectfully submit that the originally filed Figures 9A to 9B(iv), which set forth the nucleotide and protein sequences of human bcl-w and murine bcl-w, contain the same typographical errors as the original Sequence Listing. Accordingly, Applicants submit herewith substitute sheets of Figures 9A and 9B to replace the drawing sheets of Figures 9A to 9B(iv) originally filed. The substitute drawing of Figure 9B discloses the nucleotide sequence (SEQ ID NO: 6) and the encoded protein sequence (SEQ ID NO: 7) of human bcl-w. The substitute drawing of Figure 9B discloses the nucleotide sequence (SEQ ID NO: 8) and the encoded protein sequence (SEQ ID NO: 9) of murine bcl-w. These substitute sheets of drawings do not introduce new matter and are fully supported by the application as filed and by the priority document.

Turning to the claims, the Examiner rejects claims 1-4 under 35 U.S.C. §112, first paragraph as allegedly not enabled. The Examiner admits that the specification is enabling for an isolated nucleic acid molecule comprising SEQ ID NO: 6 or 8 which encodes the amino acid sequence of SEQ ID NO: 7 or 9. However, the Examiner contends that the specification does not provide enablement for all nucleic acid molecules encompassed by the claims. The Examiner states that the specification does not disclose any derivative of SEQ ID NO: 6 or 8, or a nucleic acid molecule encoding an amino acid sequence having at least 47% similarity to SEQ ID NO: 7 or 9, or a nucleic acid molecule which hybridizes under low stringency conditions to SEQ ID NO: 6 or 8 and which elicits a Bcl-w-related activity. It is the Examiner's opinion that it would take undue experimentation for those skilled in the art to practice the claimed invention.

Applicants respectfully disagree with the Examiner. Applicants respectfully submit that the present specification adequately teaches the molecules as claimed, including derivative and homologous sequences of SEQ ID NO: 6 or 8 that enhance cell survival. For example, the specification teaches the human bcl-w gene (SEQ ID NO: 6) and the murine bcl-w gene (SEQ ID NO: 8). The specification further teaches that the human Bcl-w protein and the murine Bcl-w share about 90% similarity. Moreover, the specification provides specific exemplification demonstrating that expression of the bcl-w gene enhances cell survival. See pages 35-36 of the specification. In light of the present teaching, those skilled in the art can isolate a nucleic acid molecule that either hybridizes to SEQ ID NO: 6 or 8, or encodes a protein that shares at least about 47% similarity to SEQ ID NO: 7 or 9, and determine whether the isolated molecule enhances cell survival. It is respectfully submitted that the experimentation required for those skilled in the art to make and use the claimed molecule is not undue.

However, in an effort to favorably advance the prosecution of the present case,
Applicants have canceled claims 1-4 without prejudice, rendering the rejection thereof moot.
Applicants reserve the right to pursue the subject matter of these canceled claims in a continuing application.

Applicants have also added claims 21-24, directed to nucleic acid molecules comprising SEQ ID NO: 6 or SEQ ID NO: 8, or encoding a protein having a sequence as set forth in SEQ ID NO: 7 or SEQ ID NO: 9. As the Examiner has acknowledged in the Final Action, the specification is enabling for these nucleic acid molecules.

Accordingly, withdrawal of the rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 1 and 4 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,789,201 ("the '201 patent"). According to the Examiner, the '201 patent teaches nucleotide sequences encoding a bcl-2 homolog (bcl-y). The Examiner contends that the sequence search report provided by the Examiner shows that the human bcl-y gene of the '201 patent matches 97.4% to SEQ ID NO: 6 (human bcl-w) of the claimed invention, and 85% to SEQ ID NO: 8 (murine bcl-w) of the present invention; and that the human Bcl-y protein of the '201 patent matches 98.7% to SEQ ID NO: 7 (human Bcl-w).

It is respectfully submitted that the cancellation of claims 1-4 renders the rejection moot. Withdrawal of the rejection is therefore respectfully requested.

Applicants further submit that the nucleic acid molecules of claims 21-24 are not taught by the '201 patent. Applicants have provided herewith **Exhibit B**, illustrating the differences between the bcl-w sequences of the present application and the bcl-y sequences of the '201 patent. At page 1 of Exhibit B, the human bcl-w (SEQ ID NO: 7), the murine bcl-w (SEQ ID NO: 9), the human bcl-y of the '201 patent (SEQ ID NO: 4 of the '201 patent) and the rat bcl-y of the '201 patent are compared with one another. It is observed that the human bcl-w protein of the present application differs from the human bcl-y of the '201 patent at amino acid position 15, with Ala in human bcl-w and Glu in human bcl-y. The human bcl-w protein differs from the rat bcl-y of the '201 patent at amino acid position 7 ("A" in human bcl-w and "T" in rat bcl-y), position 124 ("E" in human bcl-w and "D" in rat bcl-y), and position 128 ("A" in human bcl-w and "T" in rat bcl-y). It is further observed that the murine bcl-w protein of the present application differs from the human bcl-y of the '201 patent at amino acid position 7 ("T" in murine bcl-w and "A" in human bcl-y), position 15 ("A" in murine bcl-w and "E" in human bcl-y), and position 124 ("D" in murine bcl-w and "E" in human bcl-y). The murine bcl-w protein of

the present application also differs from the rat bcl-y of the '201 patent at amino acid position 128 ("A" in murine bcl-w and "T" in rat bcl-y). Accordingly, protein sequences of SEQ ID NO: 7 and SEQ ID NO: 9 of the present application are not taught by the '201 patent, nor are the nucleic acid molecules encoding the protein of SEQ ID NO: 7 or SEQ ID NO: 9 (i.e., the subject matter of claims 21-22) taught by the '201 patent.

At page 2 of Exhibit B, the nucleotide sequence of the human bcl-w gene (SEQ ID NO: 6 of the present application) is compared with the human bcl-y and rat bcl-y genes of the '201 patent. Those nucleotides in the bcl-y genes which differ from the human bcl-w gene are indicated underneath the human bcl-w sequence. Clearly, the human bcl-w gene (SEQ ID NO: 6) of the present application is distinct from the human bcl-y and rat bcl-y genes of the '201 patent. Therefore, claim 23, drawn to a nucleic acid molecule comprising SEQ ID NO: 6, is not taught by the '201 patent.

Page 3 of Exhibit B illustrates the differences between the murine bcl-w gene (SEQ ID NO: 8) of the present application and the bcl-y genes of the '201 patent. Clearly, the murine bcl-w gene (SEQ ID NO: 8) of the present application is distinct from the human bcl-y and rat bcl-y genes of the '201 patent. Therefore, claim 24, drawn to a nucleic acid molecule comprising SEQ ID NO: 8 is not taught by the '201 patent.

Attached hereto is a marked-up copy of the amendment to the claims and to the Sequence Listing, entitled "Version with markings to show changes made"; a substitute paper and computer-readable copy of the Sequence Listing; a statement under §1.821(f) verifying that the content of the substitute paper copy and the substitute computer-readable copy of the Sequence Listing are the same; substitute sheets for Figures 9A and Figures 9B; Exhibit A and Exhibit B.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Frank S. DiGiglio Registration No. 31,346

Scully, Scott, Murphy & Presser 400 Garden City Plaza Garden City, New York 11530 Telephone: 516-742-4343 FSD/XZ:ab

Enclosures: Marked up version of the amendment to the claims and the Sequence Listing

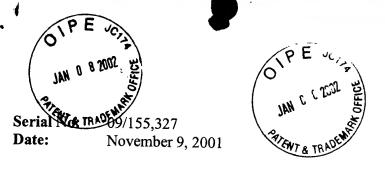
Substitute paper and computer-readable copy of the Sequence Listing

Statement under §1.821(f)

Substitute sheets of Figures 9A and 9B

Exhibit A: Priority Document (Australian Provisional Application PN8965)

Exhibit B: Comparison of bcl-w and bcl-y sequences



VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

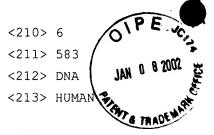
Claims 1-4 have been canceled without prejudice.

Claims 21-24 have been added:

- 21. An isolated nucleic acid molecule, wherein said nucleic acid molecule encodes a protein comprising an amino acid sequence as set forth in SEQ ID NO: 7.
- 22. An isolated nucleic acid molecule, wherein said nucleic acid molecule encodes the amino acid sequence as set forth in SEQ ID NO: 9.
- 23. An isolated nucleic acid molecule wherein said nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 6.
- 24. An isolated nucleic acid molecule wherein said nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 8.

In the Sequence Listing:

The sequences in SEQ ID NO: 6-9 have been amended as follows:



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ccc ggg gag ggc cca gca gct gac ccg ctg cac caa gcc atg cgg gca Pro Gly Glu Gly Pro Ala Ala Asp Pro Leu His Gln Ala Met Arg Ala 35 40 45

gct gga gat gag ttc gag acc cgc ttc cgg cgc acc ttc tct gat ctg 192 Ala Gly Asp Glu Phe Glu Thr Arg Phe Arg Arg Thr Phe Ser Asp Leu 50 55 60

gcg gct cag ctg cat gtg acc cca ggc tca gcc cag caa cgc ttc acc 240 Ala Ala Gln Leu His Val Thr Pro Gly Ser Ala Gln Gln Arg Phe Thr 65 75 70 80

288 cag gtc tcc gac gaa ctt ttt caa ggg ggc ccc aac tgg ggc cgc ctt Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu 90 95 85

gta gcc ttc ttt // tc ttt ggg gct gca ctg tgt gct gag agt gtc aac 336 Val Ala Phe Phe Low Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn 100 Val 105 110

aag gag atg gaa cca ctg gtg gga caa gtg cag gag tgg atg gtc 384 Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Glu Trp Met Val Ala 115 120 125

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				cgg												432
Tyr	Leu	Glu	Thr	Arg	Leu	Val	Asp	Trp	Ile	His	Ser	Ser	Gly	Gly	Trp	
_	130					135					140					
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				Ala												
	GIU	Pne	Thr	Ala		тут	Gry	nsp	Ory	155	200				160	
145					150					133					100	
															~~~	520
cgt	ctg	cgg	gag	ggg	aac	tgg	gca	tca	gtg	agg	aca	gtg	ctg	acg	ggg	528
Arg	Leu	Arg	Glu	Gly	Asn	Trp	Ala	Ser	Val	Arg	Thr	Val	Leu	Thr	Gly	
				165					170					175		
acc	ata	αca	ctq	ggg	gcc	ctg	gta	act	gta	ggg	gcc	ttt	ttt	gct	agc	576
715	77 a l	Δ1 a	ر. I.e.i	Gly	Ala	Leu	Val	Thr	Val	Gly	Ala	Phe	Phe	Ala	Ser	
MIG	Val	MIC	180					185		-			190			
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aag	tga	a														
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6	5				7	0				7	5				80	

Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu 85 90 95

Val Ala Phe Phe Lew Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn
100 105 110

Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Glu Trp Met Val Ala 115 120 125

Tyr Leu Glu Thr Arg Leu Val Asp Trp Ile His Ser Ser Gly Gly Trp

130 135 140

Arg Leu Arg Glu Gly Asn Trp Ala Ser Val Arg Thr Val Leu Thr Gly 165 170 175

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Lys

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<220>

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<222> (1)..(579)

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Phe	Val	Gly	Tyr	Arg	Leu	Arg	Gln	Lys	Gly	Tyr	Val	Cys	Gly	Ala	Gly		
			20					25					30				
							gac									144	
Pro	Gly	Glu	Gly	Pro	Ala	Ala	Asp	Pro	Leu	His	Gln	Ala	Met	Arg	Ala		
		35					40					45					
															,	100	
							cgt									192	
Ala		Asp	Glu	Phe	Glu		Arg	Phe	Arg	Arg		Pne	Ser	Asp	Leu	•	
	50				•	55					60						
			a+ a	000	ata	200	сса	aac	tca	acc	cad	caa	cac	ttc	acc	240	
							Pro										
	Ala	GIII	Leu	UTS	70	1111	110	GI,y	JCI	75	0111	01	9		80		
65					70					, 0							
cad	at.t.	tcc	gac	gaa	ctt	ttc	caa	ggg	ggc	cct	aac	tgg	ggc	cgt	ctt	288	
							Gln										
			-	85					90					95			
																	•
gtg	gca	ttc	ttt	gtc	ttt	ggg	gct	gcc	ctg	tgt	gct	gag	agt	gtc	aac	336	
Val	Ala	Phe	Phe	Val	Phe	Gly	Ala	Ala	Leu	Суѕ	Ala	Glu	Ser	Val	Asn		•
			100					105					110				
									q				9			201	
															gcc	384	
Lys	Glu	Met	Glu	Pro	Leu	Val		Gln	Val	Gln	Asp		77127	Val	Ala		
		115					120					125					
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															tgg Trp		•
Tyr			Tnr	Arg	тeп	135		TTF	110	1113	140		. 017	01	7 Trp	٠ •	
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aca	9	' ++c	· aca	act	· cta	ı tac	aac	gac	a a a	ı qcc	ctq	gaç	g ga <b>g</b>	<b>?</b> £ gca	a cgg	480	
															a Arg		
145	Glu				150		-	-	_	155			Gli	ι .	160		
											,		,				
cgt	ctg	r cgg	g gag	g gg	) / aad	tg:	g gca	tøa	a gto	g ag	aca	a gto	gøto	g aco	g ggg	528	
Arg	Leu	Arg	g Glu	ı Gly	y Asr	n Trp	o Ala	Va:	Sen	Thi	. <del>∀a]</del>	₽ Val	Thi	r Gl	y Ala	→(t, 1)	ent page)
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581 582

576

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<213> Mouse

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Ala Gly Asp Glu Phe Glu Thr Arg Phe Arg Arg Thr Phe Ser Asp Leu 50 55 60

Ala Ala Gln Leu His Val Thr Pro Gly Ser Ala Gln Gln Arg Phe Thr
65 70 75 80

Gln Val Ser Asp Glu Leu Phe Gln Gly Gly Pro Asn Trp Gly Arg Leu
85 90 95

Val Ala Phe Phe Val Phe Gly Ala Ala Leu Cys Ala Glu Ser Val Asn 100 105 110

Lys Glu Met Glu Pro Leu Val Gly Gln Val Gln Asp Trp Het Val Ala
115 120 125

Tyr Leu Glu Thr Arg Leu Ala Asp Trp Ile His Ser Ser Gly Gly Trp 130 135 140

Ala Asp Phe Thr Ala Leu Tyr Gly Asp Gly Ala Leu Glu Asp Ala Arg

145

150

160

145

Arg Leu Arg Glu Gly Asn Trp Ala Val Ser Thr Val Val Thr Gly

165

170

Ala Val Ala Leu Gly Ala Leu Val Thr Val Gly Ala Phe Phe Ala Ser 180 185

Lys

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														gct Ala		96
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aag Lys	tga	a														583

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